REMARKS

Reconsideration and withdrawal of the rejections of the claims, in view of the amendments and remarks presented herein, is respectfully requested. Claims 2-3, 5-8 and 17-20 are amended. Claims 1, 4, 9, 10, and 16 are cancelled. Claim 22-26 are newly added. As a result, claims 2-3, 5-8, and 11-15, 17-26 are now pending in this application.

The amendments to the claims have been made to expedite prosecution of the present application. The amendments to the claims are fully supported by the specification as originally filed, and no new subject matter has been added.

Support for the amendment to claims 6, 7, 18 and 19 is found at page 3, lines 14-16 of the specification.

Support for the amendment to claim 8 is found at page 1, lines 24-27 and in Examples 1-3 of the specification, and in originally filed claim 16.

Support for new claims 22-26 is found in claim 4 as originally filed.

Information Disclosure Statement

Applicants respectfully request that the Supplemental Information Disclosure Statement (S-IDS) that was filed October 11, 2002, be entered and the documents listed on the attached Form 1449 be considered by the Examiner and made of record. For the Examiner's convenience, a copy of the S-IDS is enclosed herewith, as well as a copy of the date stamped return postcard filed with the S-IDS. "A postcard receipt which itemizes and properly identifies the items which are being filed serves as *prima facie* evidence of receipt in the U.S.P.T.O. of all the items listed thereon on the date stamped thereon by the U.S.P.T.O." M.P.E.P. § 503. Applicants further request that a copy of the Form 1449 be initialed by the Examiner to indicate that all listed citations have been considered, and be returned to Applicants' Representatives with the next official communication.

The 35 U.S.C. § 112 Rejections of the Claims

Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 6-7 and 18-19 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner asserts that the length of the oligonucleotides of claims 6-7 and 18-19 indefinite. As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

As amended, the claims are directed to an oligonucleotide comprising an antisense nucleic acid sequence that specifically binds to a nucleic acid encoding a human antioxidant enzyme start codon, wherein the antisense sequence is about 18 to 26 nucleotides in length, and wherein the antioxidant enzyme is manganese superoxide dismutase, copper and zinc superoxide dismutase, catalase, phospholipid glutathione peroxidase, or cytosolic glutathione peroxidase, wherein the antisense nucleic acid sequence is 90% complementary to a portion of the nucleic acid encoding an antioxidant enzyme (claim 6); and wherein the antisense nucleic acid sequence is 100% complementary to a portion of the nucleic acid encoding an antioxidant enzyme (claim 7); and to a method of treating a tumor in a mammal comprising reducing antioxidant enzyme levels in a cell by administering a therapeutic agent comprising an antisense nucleic acid sequence that specifically binds to a nucleic acid encoding a human antioxidant enzyme start codon, wherein the antisense sequence is about 18 to 26 nucleotides in length, wherein the antisense nucleic acid sequence is 90% complementary to a portion of the nucleic acid encoding an antioxidant enzyme (claim 18); and wherein the antisense nucleic acid sequence is 100% complementary to a portion of the nucleic acid encoding an antioxidant enzyme (claim 19).

It is well-settled that claim language is sufficiently definite if one of ordinary skill in the art would understand the scope of the claim when read in light of the specification. *In re Marosi*, 710 F.2d 799, 218 U.S.P.Q. 289 (Fed. Cir. 1983); *Morton Inst. Inc. v. Cardinal Chemical Co.*, 28 U.S.P.Q.2d 1190 (Fed. Cir. 1993); *Miles Laboratories v. Shandon Inc.*, 27 U.S.P.Q.2d 1123 (Fed. Cir. 1993), *cert. denied*, 510 U.S. 1100 (1994). The phrase "complementary to a portion of nucleic acid" as recited in amended claims 6-7 and 18-19 is conventional and understood in the art. *See*, for example, Green et al., *J. Am Coll. Surg.*, *191*, 93-105 (2000), a copy of which is

attached hereto. At page 93, left hand column and at page 95, right hand column, Green et al. disclose that antisense oligodeoxyribonucleotides complementary to a segment of mRNA can be used to inhibit gene expression in antisense technology. With respect to the term "segment," the Examiner is respectfully requested to consider page 2056 of Webster's Third New International Dictionary of the English Language Unabridged, (Merriam-Webster Inc., Springfield, Mass. USA (1993) (a copy of which is enclosed herewith). At page 2056, it is disclosed that "segment" means "a piece or separate fragment of something: portion." Therefore, the metes and bounds of a claim that recites a certain percentage of complementary to a portion of nucleic acid would be readily recognized and understood by the art worker in possession of the specification.

Therefore, withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Rejections under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 1-19 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains that the inventor at the time the application was filed, had possession of the claimed invention (written description). In particular, the Examiner asserts that the present claims encompass targeting "any" start codon of "any" catalase, copper and zinc superoxide dismutase, manganese superoxide dismutase, phospholipid or cytosolic glutathione peroxidase or "any allele, mutant and homolog from any species" (page 4 of the Office Action). This rejection, as it may be maintained with respect to the pending claims, is respectfully traversed.

Claims 1, 4, 9 and 10 have been cancelled, and claims 2-3, 5-8 and 18-19 have been amended. Insofar as the rejection is applied to the pending claims, it is hereby traversed.

Possession of a claimed invention may be shown through disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, *Federal Register*, *66*, 1099, 1106 (January 5, 2001).

The pending claims, as amended, are directed to an oligonucleotide comprising an antisense nucleic acid sequence that specifically binds to a nucleic acid encoding a human antioxidant enzyme start codon, wherein the antisense sequence is about 18 to 26 nucleotides in length, and wherein the antioxidant enzyme is manganese superoxide dismutase, copper and zinc superoxide dismutase, catalase, phospholipid glutathione peroxidase, or cytosolic glutathione peroxidase, wherein the antisense nucleic acid sequence is 90% or 100% complementary to a portion of the nucleic acid encoding an antioxidant enzyme (claims 2, 3, 5-7) or a method of treating a tumor in a mammal comprising reducing antioxidant enzyme levels in a cell by administering a therapeutic agent comprising an antisense nucleic acid sequence that specifically binds to a nucleic acid encoding a human antioxidant enzyme start codon, wherein the antisense sequence is about 18 to 26 nucleotides in length (claims 8 and 11-19).

The Examiner is respectfully requested to consider that, as amended, Applicants' pending claims are not directed to oligonucleotides comprising nucleic acid sequences that specifically bind to the start codon of an antioxidant enzyme of "any" species, but to oligonucleotides comprising nucleic acid sequences that specifically bind to the start codons of particular human antioxidant enzymes, *viz.*, manganese super oxide dismutase (MnSOD), copper and zinc superoxide dismutase, catalase (CAT), phospholipid glutathione peroxidase (GPx), and cytosolic GPx. Page 3, line 27 through page 4, line 27 of the present specification discloses examples of oligonucleotide constructs that specifically bind to the mRNA start codons, *i.e.*, to AUG, of MnSOD (SEQ ID Nos: 1-3), CAT (SEQ ID Nos: 4-5) and phospholipid GPx (SEQ ID Nos: 6-7). As evidence that the art worker, at the time the present application was filed, was apprized of the coding sequences for copper and zinc superoxide dismutase and cytosolic GPx, the Examiner is respectfully requested to consider GenBank Accession Numbers X02317, M21304 and AF199441 (a copy of each is enclosed herewith for the Examiner's convenience). Thus, adequate description of the targets for the antisense sequences was either specifically taught by the specification and/or was known by those having skill in the art at the time the application was filed. Further, these claimed oligonucleotides have particular structural features, such as being about 18 to 26 nucleotides in length and optionally being 90% or 100% complementary to a portion of the nucleic acid encoding an antioxidant enzyme.

Thus, Applicant has provided adequate written description for the pending claims. Applicant requests that this rejection under 35 U.S.C. § 112, first paragraph (written description) be withdrawn.

Rejections under 35 U.S.C. § 112, First Paragraph – Scope of Enablement

Claims 8 and 11-19 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (scope of enablement). As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

As amended, claim 8 is directed to a method of treating a tumor in a mammal comprising reducing antioxidant enzyme levels in a cell by administering a therapeutic agent comprising an antisense nucleic acid sequence that specifically binds to a nucleic acid encoding a human antioxidant enzyme start codon, wherein the antisense sequence is about 18 to 26 nucleotides in length, and wherein the antioxidant enzyme is manganese superoxide dismutase, copper and zinc superoxide dismutase, catalase, phospholipid glutathione peroxidase, or cytosolic glutathione peroxidase. Claims 11-19 are dependent upon claim 8.

As evidence that Applicant's invention is enabled, the Examiner is respectfully requested to consider Applicant's detailed description. To produce an oligonucleotide comprising an antisense nucleic acid that specifically binds to (i) a nucleic acid encoding a human MnSOD mRNA start codon; (ii) a nucleic acid encoding a human copper and zinc superoxide dismutase enzyme mRNA start codon; (iii) a nucleic acid encoding a human CAT enzyme mRNA start codon; (iv) a nucleic acid encoding a human phospholipid GPx enzyme mRNA start codon; or (v) a nucleic acid encoding a human cytosolic glutathione peroxidase mRNA start codon, Applicant discloses that 20-mer sequences can be produced synthetically with the start codon of the particular enzyme in the center of the oligonucleotide (page 3, lines 31-33). Additional oligonucleotides can also be prepared, wherein the start sequence is shifted in either the 5′ or 3′ direction (page 3, line 33-page 4, line 1).

For example, as discussed above, Applicant discloses that oligonucleotides comprising antisense nucleic acid sequences that specifically bind to nucleic acid encoding the human MnSOD mRNA start codon were prepared (page 4, lines 1-11) as well oligonucleotides comprising antisense nucleic acid sequences that specifically bind nucleic acid encoding human CAT and human phospholipid GPx mRNA start codon (page 4, lines 14-25).

To determine whether the administration of an oligonucleotide of the invention reduces the level of antioxidant enzyme in a cell, Applicant discloses a candidate oligonucleotide can be added to tissue culture cells, *e.g.*, human cancer cells such as MCF10A or MCF-7 breast cancer cells. Following a period of incubation, the cells can be harvested, and a Western blot analysis can be conducted to determine whether or not the level of antioxidant enzyme is reduced (Examples1-3).

Therefore, it is respectfully submitted that the pending claims are in conformance with 35 U.S.C. § 112, first paragraph (enablement). Thus, withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, is respectfully requested.

The 35 U.S.C. §102(b) Rejection of the Claims

The Examiner rejected claims 1-2 under 35 U.S.C. § 102(b) as being anticipated by Sugino *et al.*, *Biology of Reprod.*, *61*, 1133-1138 (1999).

The standard for anticipation is one of strict identity, and to anticipate a claim for a patent a single prior art source must contain all its elements. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q.2d 90 (Fed. Cir. 1986); *In re Dillon*, 16 U.S.P.Q.2d 1987 (Fed. Cir. 1990). Furthermore, there must be no difference between the claimed invention and the disclosure, as viewed by a person of ordinary skill in the art. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 18 U.S.P.Q.2d 1001 (Fed. Cir. 1991).

Claim 1 has been cancelled. Claim 2 has been amended to depend from claims 6 or 7, which the examiner indicated are free of the cited art.

Therefore, withdrawal of this rejection under 35 U.S.C. § 102(b) is respectfully requested.

Rejection of the Claims under 35 U.S.C. §103(a)

The Examiner rejected claims 1, 2, 3 and 5 under 35 U.S.C. § 103(a) as being unpatentable over either of Ferguson-Kohout *et al.*, *FASEB J.*, *10*, 3067 (1996), or Bauman *et al.*, *Teratology*, *53*, 84 (1996), in view of Baracchini *et al.* (U.S. Patent No. 5,801,154). As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

Claim 1 has been cancelled. Claims 2, 3 and 5 have been amended to depend from claims 6 or 7, which the examiner indicated are free of the cited art.

Therefore, this rejection under 35 U.S.C. § 103(a) should be withdrawn.

Allowable Subject Matter

At page 8 of the final Office Action, the Examiner indicated that claims 20-21 would be allowable if rewritten to delete withdrawn subject matter, *i.e.*, SEQ ID NO:1 and SEQ ID NO:3, as a sequence search has revealed no prior art against SEQ ID NO:2. Claim 20 is an independent claim, and claim 21 depends from claim 20. Claim 20 has been as suggested by the examiner. Therefore, claims 20 and 21 should now be allowable.

Conclusion

Applicants respectfully submit that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicants' attorney (612-373-6961) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

LARRY WAYNE OBERLEY ET AL.,

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6961

Date 21 October 2003 By Ann S. Viksnins

Ann S. Viksnins
Reg. No. 37,748

CERTIFICATE UNDER 37 C.F.R. 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 21st day of October, 2003.

Name Candis B. Buending

Signature Candis B. Buending